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Ulf Gyllensten

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24256 7590 10/27/2008  
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EXAMINER

THOMAS, DAVID C

ART UNIT

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1637

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PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/529,447	<b>Applicant(s)</b> GYLLENSTEN ET AL.	
	<b>Examiner</b> DAVID C. THOMAS	<b>Art Unit</b> 1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 05 August 2008.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 9-14 and 18-26 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 9-14 and 18-26 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                     | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____  | 6) <input type="checkbox"/> Other: _____                          |

### **DETAILED ACTION**

1. Applicant's amendment filed August 5, 2008 is acknowledged. Claims 9-14 and 18-20 (original or previously presented) and 21-26 (newly presented) will be examined on the merits. Claims 1-8 and 15-17 were previously canceled.

### ***Claim Rejections - 35 USC § 103***

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

3. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

4. Claims 9 and 21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kroeger et al. (U.S. Patent Pub. No. 2002/0137021) in view of Gissmann et al. (U.S. Patent No. 6,228,368) and further in view of Goldsborough et al. (GenBank Accession No. J04353, 1994) and further in view of Seedorf et al. (EMBO J. (1987) 6:139-144) and

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further in view of Sastre-Garau et al. (J. Gen. Virol. (2000) 81:1983-1993 and GenBank Accession No. AJ242956) and further in view of Buck et al. (BioTechniques (1999) 27:528-536).

With regard to claims 9 and 21, Kroeger teaches a kit for detecting oncogenic HPV, including HPV 16, 18, 31 and 45 (see Table 1 on p. 2), the kit comprising primers and probes that can be used in a cocktail for amplification and detection of multiple HPV types at once (paragraph 6, lines 1-12, paragraph 7, lines 1-26 and paragraph 24, lines 1-8).

Kroeger does not teach a kit comprising the amplification primers of SEQ ID NOS: 1-8, and the probes of SEQ ID NOS: 21-24, for detection of HPV 16, 18, 31, 35 and 45, wherein the primers and probes specific for HPV 16 detect a sequence in the E7 open reading frame, the primers and probes specific for HPV 18 and 45 detect a sequence in the E1 open reading frame, and the primers and probes specific for HPV 31 detect a sequence in the E6 open reading frame.

With regard to claim 9, Gissmann teaches a sequence within the E7 open reading frame of HPV 16 that can be used for designing primers SEQ ID NO: 1 and SEQ ID NO: 2, and the probe SEQ ID NO: 21 for detection and quantification of HPV 16 (positions 91-111 of SEQ ID NO: 3 of Gissmann is homologous to SEQ ID NO: 1, positions 168-146 of SEQ ID NO: 3 of Gissmann is homologous to SEQ ID NO: 2, and positions 121-142 of SEQ ID NO: 3 of Gissmann is homologous to SEQ ID NO: 21).

With regard to claim 9, Goldsborough teaches a sequence within the E6 open reading frame of HPV 31 that can be used for designing primers SEQ ID NO: 3 and SEQ ID NO: 4 and the probe SEQ ID NO: 22 for detection and quantification of HPV 31 (positions 476-497 of J04353 of Goldsborough is homologous to SEQ ID NO. 3, positions 556-533 of J04353 is homologous to SEQ ID NO: 4, and positions 529-507 of J04353 is homologous to SEQ ID NO: 22).

With regard to claim 9, Seedorf teaches a sequence within the E1 open reading frame of HPV 18 that can be used for designing primers SEQ ID NO: 5-7 and the probe SEQ ID NO: 23 and 24 for detection and quantification of HPV 18 (positions 1093-1113 of Seedorf, Figure 1a is homologous to SEQ ID NO: 5/6, positions 1168-1148 is homologous to SEQ ID NO: 7, and positions 1115-1140 is homologous to SEQ ID NO: 23/24).

With regard to claim 9, Sastre-Garau teaches a sequence within the E1 open reading frame of HPV 45 that can be used for designing primer SEQ ID NO: 8 for detection and quantification of HPV 45 (positions 7185-7164 of AJ242956 of Sastre-Garau is homologous to SEQ ID NO: 8).

It would have been prima facie obvious to one having ordinary skill in the art at the time the invention was made to utilize the sequences taught by Gissmann, Goldsborough, Seedorf and Sastre-Garau in order to design amplification primers and probes for a kit to detect and quantify HPV in a type-specific manner, as taught by Kroeger. Thus, an ordinary practitioner would have been motivated to use such sequences in order to design primers and probes that are specific for particular HPV

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types, especially high-risk types such as HPV 16, 18, 31 and 45 associated with cervical cancer. Such a kit provides the necessary primers, probes and other amplification reagents to form cocktails that can detect multiple HPV types in a single amplification reaction (Kroeger, paragraph 7, lines 11-23 and paragraph 24, lines 1-8).

In the recent court decision *KSR International Co. v. Teleflex Inc.*, 82 127 SCt 1727 (2007), the U.S. Supreme Court determined that if the combination of the claimed elements was “obvious to try” by a person of ordinary skill, this might show that such a combination was obvious under §103. Regarding “obvious to try”, the Court stated:

“A person of ordinary skill is also a person of ordinary creativity, not an automaton. The same constricted analysis led the Court of Appeals to conclude, in error, that a patent claim cannot be proved obvious merely by showing that the combination of elements was “obvious to try.” *Id.*, at 289 (internal quotation marks omitted). When there is a design need or market pressure to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense. In that instance the fact that a combination was obvious to try might show that it was obvious under §103.”

Since the claimed primers simply represent structural homologs of the oligonucleotides taught by Gissmann, Goldsborough, Seedorf and Sastre-Garau, which are 100% derived from sequences expressly suggested by the prior art of Gissmann, Goldsborough, Seedorf and Sastre-Garau as useful for primers for the detection and quantification of human papillomavirus, and concerning which a biochemist of ordinary skill would attempt to obtain alternate compounds with improved properties, the claimed primers are *prima facie* obvious over the cited references in the absence of secondary considerations.

With regard to the issue of equivalence of the primers, MPEP 2144.06 notes “Substituting equivalents known for the same purpose. In order to rely on equivalence as a rationale supporting an obviousness rejection, the equivalency must be recognized in the prior art, and cannot be based on applicant's disclosure or the mere fact that the components at issue are functional or mechanical equivalents. An express suggestion to substitute one equivalent component or process for another is not necessary to render such substitution obvious. In re Fout , 675 F.2d 297, 213 USPQ 532 (CCPA 1982).”

With regard to the issue of reasonable expectation of success in using such equivalents, Buck expressly provides evidence of the equivalence of primers. Specifically, Buck invited primer submissions from a number of labs (39) (page 532, column 3), with 69 different primers being submitted (see page 530, column 1). Buck also tested 95 primers spaced at 3 nucleotide intervals along the entire sequence at issue, thereby testing more than 1/3 of all possible 18 mer primers on the 300 base pair sequence (see page 530, column 1). When Buck tested each of the primers selected by the methods of the different labs, Buck found that EVERY SINGLE PRIMER worked (see page 533, column 1). Only one primer ever failed, No. 8, and that primer functioned when repeated. Further, EVERY SINGLE CONTROL PRIMER functioned as well (see page 533, column 1). Buck expressly states “The results of the empirical sequencing analysis were surprising in that nearly all of the primers yielded data of extremely high quality (page 535, column 2).” Therefore, Buck provides direct evidence that all primers would be expected to function, and in particular, all primers selected

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according to the ordinary criteria, however different, used by 39 different laboratories. It is particularly striking that all 95 control primers functioned, which represent 1/3 of all possible primers in the target region. This clearly shows that every primer would have a reasonable expectation of success.

5. Claims 10, 11, 22 and 23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kroeger et al. (U.S. Patent Pub. No. 2002/0137021) in view of Gissmann et al. (U.S. Patent No. 6,228,368) and further in view of Goldsborough et al. (GenBank Accession No. J04353, 1994) and further in view of Seedorf et al. (EMBO J. (1987) 6:139-144) and further in view of Sastre-Garau et al. (J. Gen. Virol. (2000) 81:1983-1993 and GenBank Accession No. AJ242956) and further in view of Buck et al. (BioTechniques (1999) 27:528-536) as applied to claim 9 above, and further in view of Yoo et al. (Genomics (1993) 15:21-29 and GenBank Accession No. M95623).

Kroeger, Gissmann, Goldsborough, Seedorf, Sastre-Garau and Buck together teach the limitations of claims 9 and 21 as discussed above.

Neither Kroeger, Gissmann, Goldsborough, Seedorf, Sastre-Garau nor Buck teach amplification primers SEQ ID NO:19 and SEQ ID NO:20 and the probe SEQ ID NO:30, for detection and quantification of the amount of the human single copy gene hydroxymethylbilane synthase (HUMPBGDA).

With regard to claims 10, 11, 22 and 23, Yoo teaches a sequence that can be used for designing primers SEQ ID NO:19 and SEQ ID NO:20, and the probe SEQ ID NO:30 for detection and quantification of the human single copy gene HUMPBGDA

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(positions 4750-4770 of the PBGD sequence taught by Yoo is homologous to SEQ ID NO. 19, positions 4868-4850 of Yoo is homologous to SEQ ID NO. 20, and positions 4788-4813 of Yoo is homologous to SEQ ID NO. 30).

It would have been prima facie obvious to one having ordinary skill in the art at the time the invention was made to include in the kit taught by Kroeger, Gissmann, Goldsborough, Seedorf, Sastre-Garau and Buck, the additional sequences taught by Yoo in order to design amplification primers and probes for the kit to detect and quantitate HUMPBGDA, used as a reference gene for quantification purposes. Thus, an ordinary practitioner would have been motivated to use such sequences in order to design primers and probes that are specific for a single-copy human PBGD gene which can be used for determining cell-copy number for more accurate detection and quantification of human papillomavirus such as the high-risk types of HPV 16, 18, 31 and 45 associated with cervical cancer.

In the recent court decision *KSR International Co. v. Teleflex Inc.*, 82 127 SCt 1727 (2007), the U.S. Supreme Court determined that if the combination of the claimed elements was “obvious to try” by a person of ordinary skill, this might show that such a combination was obvious under §103. Regarding “obvious to try”, the Court stated:

“A person of ordinary skill is also a person of ordinary creativity, not an automaton. The same constricted analysis led the Court of Appeals to conclude, in error, that a patent claim cannot be proved obvious merely by showing that the combination of elements was “obvious to try.” *Id.*, at 289 (internal quotation marks omitted). When there is a design need or market pressure to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense. In that instance the fact that a combination was obvious to try might show that it was obvious under §103.”

Since the claimed primers simply represent structural homologs of the oligonucleotides taught by Yoo, which are 100% derived from sequences expressly suggested by the prior art of Yoo as useful for primers for the detection and quantification of human PBGD and concerning which a biochemist of ordinary skill would attempt to obtain alternate compounds with improved properties, the claimed primers are *prima facie* obvious over the cited references in the absence of secondary considerations.

With regard to the issue of equivalence of the primers, MPEP 2144.06 notes “Substituting equivalents known for the same purpose. In order to rely on equivalence as a rationale supporting an obviousness rejection, the equivalency must be recognized in the prior art, and cannot be based on applicant's disclosure or the mere fact that the components at issue are functional or mechanical equivalents. An express suggestion to substitute one equivalent component or process for another is not necessary to render such substitution obvious. In re Fout , 675 F.2d 297, 213 USPQ 532 (CCPA 1982).”

With regard to the issue of reasonable expectation of success in using such equivalents, Buck expressly provides evidence of the equivalence of primers. Specifically, Buck invited primer submissions from a number of labs (39) (page 532, column 3), with 69 different primers being submitted (see page 530, column 1). Buck also tested 95 primers spaced at 3 nucleotide intervals along the entire sequence at issue, thereby testing more than 1/3 of all possible 18 mer primers on the 300 base pair sequence (see page 530, column 1). When Buck tested each of the primers selected

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by the methods of the different labs, Buck found that EVERY SINGLE PRIMER worked (see page 533, column 1). Only one primer ever failed, No. 8, and that primer functioned when repeated. Further, EVERY SINGLE CONTROL PRIMER functioned as well (see page 533, column 1). Buck expressly states "The results of the empirical sequencing analysis were surprising in that nearly all of the primers yielded data of extremely high quality (page 535, column 2)." Therefore, Buck provides direct evidence that all primers would be expected to function, and in particular, all primers selected according to the ordinary criteria, however different, used by 39 different laboratories. It is particularly striking that all 95 control primers functioned, which represent 1/3 of all possible primers in the target region. This clearly shows that every primer would have a reasonable expectation of success.

6. Claims 12, 14, 24 and 26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kroeger et al. (U.S. Patent Pub. No. 2002/0137021) in view of Gissmann et al. (U.S. Patent No. 6,228,368) and further in view of Goldsborough et al. (GenBank Accession No. J04353, 1994) and further in view of Seedorf et al. (EMBO J. (1987) 6:139-144) and further in view of Sastre-Garau et al. (J. Gen. Virol. (2000) 81:1983-1993 and GenBank Accession No. AJ242956) further in view of Buck et al. (BioTechniques (1999) 27:528-536) as applied to claim 9 above, and further in view of Swan et al. (J. Clin. Microbiol. (1997) 35:886-891).

Kroeger, Gissmann, Goldsborough, Seedorf, Sastre-Garau and Buck together teach the limitations of claims 9 and 21 as discussed above.

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Neither Kroeger, Gissmann, Goldsborough, Seedorf, Sastre-Garau nor Buck teach a kit comprising at least two different fluorophores for detection and diagnosis of cervical cancer.

With regard to claims 12, 14, 24 and 26, Swan teaches a type-specific fluorogenic probe assay for detection and quantification of HPV, including high-risk types associated with cervical cancer, using probes containing FAM or HEX and a rhodamine quencher dye, TAMRA (p. 886, column 1, lines 1-5, lines and column 2, lines 7-25).

It would have been prima facie obvious to one having ordinary skill in the art at the time the invention was made to combine the teachings of Kroeger, Gissmann, Goldsborough, Seedorf, Sastre-Garau and Buck that disclose sequences to allow designing of primers and probes for a kit for detection and quantification of HPV 16, 18, 31 and 45 with those of Swan that teach the use of fluorogenic probes for detecting and quantifying high-risk HPV types since the probes can all be readily prepared with fluorescent labels during synthesis using the necessary phosphoramidites and esters (Swan, p. 886, column 2, lines 16-25). Thus, an ordinary practitioner would have been motivated to use HPV sequences in order to design primers and fluorescently-labeled probes to provide a kit for performing a fast, simple and highly sensitive detection method for typing HPV DNA, since the probe is present in the PCR reaction mixture to allow direct measurement of fluorescence after PCR without further manipulations (Swan, p. 890, column 1, line 13 to column 2, line 5).

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7. Claims 13, 18-20 and 25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kroeger et al. (U.S. Patent Pub. No. 2002/0137021) in view of Gissmann et al. (U.S. Patent No. 6,228,368) and further in view of Goldsborough et al. (GenBank Accession No. J04353, 1994) and further in view of Seedorf et al. (EMBO J. (1987) 6:139-144) and further in view of Sastre-Garau et al. (J. Gen. Virol. (2000) 81:1983-1993 and GenBank Accession No. AJ242956) and further in view of Buck et al. (BioTechniques (1999) 27:528-536) and further in view of Yoo et al. (Genomics (1993) 15:21-29 and GenBank Accession No. M95623) as applied to claims 10 and 11 above, and further in view of Swan et al. (J. Clin. Microbiol. (1997) 35:886-891).

Kroeger, Gissmann, Goldsborough, Seedorf, Sastre-Garau, Buck and Yoo together teach the limitations of claims 10, 11, 22 and 23 as discussed above.

Neither Kroeger, Gissmann, Goldsborough, Seedorf, Sastre-Garau, Buck nor Yoo teach a kit comprising three different fluorophores for detection and diagnosis of cervical cancer.

With regard to claims 13, 18-20 and 25, Swan teaches a type-specific fluorogenic probe assay for detection and quantification of HPV, including high-risk types associated with cervical cancer, using probes containing FAM or HEX and a rhodamine quencher dye, TAMRA (p. 886, column 1, lines 1-5, lines and column 2, lines 7-25).

It would have been prima facie obvious to one having ordinary skill in the art at the time the invention was made to combine the teachings of Kroeger, Gissmann, Goldsborough, Seedorf, Sastre-Garau, Buck and Yoo that teach sequences to allow designing of primers and probes for a kit for detection and quantification of HPV 16, 18,

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31 or 45 as well as that of a house-keeping gene, PBGD, with those of Swan that teach the use of fluorogenic probes for detecting and quantifying high-risk HPV types since the HPV and PBGD probes can all be readily prepared with fluorescent labels during synthesis using the necessary phosphoramidites and esters (Swan, p. 886, column 2, lines 16-25). Thus, an ordinary practitioner would have been motivated to use HPV and PBGD sequences in order to design primers and fluorescently-labeled probes to provide a kit for performing a fast, simple and highly sensitive detect method for typing HPV DNA, since the probe is present in the PCR reaction mixture to allow direct measurement of fluorescence after PCR without further manipulations (Swan, p. 890, column 1, line 13 to column 2, line 5). Furthermore, primers and a probe for a housekeeping gene such as PBGD or  $\beta$ -globin (used by Swan) can be used to normalize the HPV signal to improve quantification, since this allows samples with unequal DNA content or reaction inhibitors to be measured accurately (Swan, p. 890, column 2, lines 28-36).

### ***Response to Arguments***

8. Applicant's arguments filed August 5, 2008 have been fully considered but they are not persuasive.

Applicant argues that the rejection of claim 9 under 35 U.S.C. 103(a) over Kroeger et al. (U.S. Patent Pub. No. 2002/0137021) in view of Gissman et al. (U.S. Patent No. 6,228,368) and further in view of Goldsborough et al. (GenBank Accession No. J04353, 1994) and further in view of Seedorf et al. (EMBO J. (1987) 6:139-144) and

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further in view of Sastre-Garau et al. (J. Gen. Virol. (2000) 81:1983-1993 and GenBank Accession No. AJ242956) and further in view of Buck et al. (BioTechniques (1999) 27:528-536) should be withdrawn since the combination of the references does not teach or suggest a kit as defined in the claim, or improvements provided by said kit, for detection and quantification of HPV. In addition, Applicant argues that the rejection of claims 10 and 11 under 35 U.S.C. 103(a) over Kroeger in view of Gissman and further in view of Goldsborough and further in view of Seedorf, Sastre-Garau, Buck and Yoo (Genomics (1993) 15:21-29 and GenBank Accession No. M95623), as well as claims 12 and 14 over Kroeger in view of Gissman and further in view of Goldsborough and further in view of Seedorf, Sastre-Garau, Buck and Swan (J. Clin. Microbiol. (1997) 35:886-891) and claims 13 and 18-20 over Kroeger in view Gissman and further in view of Goldsborough and further in view of Seedorf, Sastre-Garau, Buck, Yoo and Swan, all dependent from claim 9, should also be withdrawn since the combination of the references does not teach or suggest every element of the base claim.

In particular, Applicant argues that, based on the passage on page 2, beginning on line 24 of the specification, the kit of the present invention has the advantage of detecting and quantifying the HPV types most commonly detected in cervical tumors while minimizing the number of parallel reactions performed for each sample. The Examiner asserts that the detection and quantification of different HPV types results not from the kit itself, but from the use of the kit components in specific process steps that are not under consideration in the instant claims. Thus, any functional characteristics of the kit components, such as detecting HPV types in a minimum number of reactions

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using combinations of primers and probes without competition among the reagents to avoid hindrances to an efficient PCR for balanced co-amplification, represents an intended use of the product and thus does not carry weight for examination of the product claims. Furthermore, there are no specific guidelines in the claims or the specification for how the kit components are configured, and thus while combinations of multiple primers and probes are used in detection assays, there is no teaching that requires the components of the kit to be packaged as combinations, but could in fact be packaged individually and later combined for use in the detection assays. Therefore, the kit components, whether packaged as cocktails or individually, can be treated as separate products, not as a mixture of products in a single container such as a reaction vessel.

Applicant further argues that Kroeger, while teaching primer and probe sequences useful for detecting HPV types in a test sample, the sequences are significantly different from those required in claim 9. In particular, Applicant argues that Kroeger teaches the use of probe sequences that hybridize within a similar region of the HPV genome, unlike the primers and probes of the instant invention that amplify different reading frames and therefore provide for balanced co-amplification. Applicant also argues that the secondary references, while teaching specific primer or probe sequences, do not teach the combination of primers and probes that may comprise a kit for detecting multiple types of HPV by amplifying the said different reading frames resulting in the stated balanced co-amplification and further argues that there is no motivation to combine the various teachings to provide a kit to obtain such a

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functionality. Applicant further argues that it would not be "obvious to try" the various oligonucleotides suggested by the secondary references in combination with the teaching of Kroeger since there are not "a finite number of identified, predictable solutions" to a design need or market pressure. As stated above, Kroeger provides motivation to combine multiple primers and probes in a kit since this reference teaches a kit that not only contains multiple components for amplification, but that such components can be used for simultaneous detection of multiple HPV types. The Examiner also asserts that one of ordinary skill in the art would be able to design a reasonable number of primer and probe sequences from the sequences taught by the cited references using primer and probe design software available at the time the invention was made that would have a reasonable chance of success of detecting type-specific HPV sequences. Based on the teachings of Kroeger, the skilled practitioner would also have been able to combine one or more sets of reagents to arrive at a kit for detecting multiple HPV types.

Therefore, based on all the issues discussed above, the rejections of claims 9-14 and 18-20, as well as new claims 21-26, under 35 U.S.C. 103(a) are maintained.

### ***Summary***

9. Claims 9-14 and 18-26 are rejected. No claims are allowable.

### ***Conclusion***

10. **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

### ***Correspondence***

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to David C. Thomas whose telephone number is 571-272-3320 and whose fax number is 571-273-3320. The examiner can normally be reached on 5 days, 9-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR.

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Status information for unpublished applications is available through Private PAIR only.

For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/David C Thomas/  
Examiner, Art Unit 1637

/Kenneth R Horlick/  
Primary Examiner, Art Unit 1637